

## Poster abstract for the 1997 Pacific Symposium on Biocomputing

**Title:** Computer-aided design of a proton pump

**Authors:** Michael H. New and Andrew Pohorille

### **Abstract:**

The use of transmembrane proton gradients in energy transduction is an almost universal feature of life on earth. These proton gradients are established and maintained by specialized assemblies of proteins which actively pump protons across membranes. One broad class of proton pumps uses captured light energy to drive the proton pumping. Our goal is to elucidate the minimum structural requirements of a light-driven proton-pump.

There are two basic components to a simple light-driven proton pump: a source of photo-generated protons and a "gate-keeper" which prevents these protons from re-attaching themselves to their source. A wide variety of molecules in the membrane, even as simple as polycyclic aromatic hydrocarbons,<sup>1</sup> are capable of releasing protons when illuminated. Our work is therefore focused on the design of the "gate-keeper." Our initial model involves a pair of proton acceptors, coupled to each other by a transient water bridge, and supported in the membrane by a small bundle of peptide helices.<sup>2</sup> Upon illumination, the proton source transfers its proton to the first acceptor of the gate-keeper. While the reverse reaction is highly probable, all that is needed to ensure irreversibility is a nonvanishing probability that the proton will be transferred to the second acceptor across a transient water bridge. Back transfer of the proton to the first acceptor, and thence to the proton source, is impeded by the free energy required to move the proton uphill towards the proton source and by the disruption of the transient water bridge.

As a prototypical water-bridged proton transfer system, we are studying the transfer of a proton across a water bridge from a formic acid to a formate anion. With a  $pK_a$  of 3.7, formic acid is a good model for the acidic amino acids glutamate and aspartate which are good candidates for gate-keeper proton acceptors.

Simulations of proton transfer reactions in a membrane are complicated by the quantum mechanical nature of the process breaking and forming chemical bonds.